

**REMARKS**

The specification has been amended to insert --This application is a national stage entry under 35 U.S.C. § 371 of PCT/JP99/06491, filed on November 19, 1999--, following the Title. However, this application is a national stage entry of PCT/JP99/06491, and does not claim benefit of a copending non-provisional application or international application designating the United States. The amendment is unnecessary, but offered herein to advance prosecution.

Claim 1 has been amended to recite one specific compound, i.e., 5-chloro-2-(1-homopiperazinyl)-7-methylbenzoxazole. This amendment is supported by the specification, for example, Example 1.

Claims 18-24 have been added as new claims. Claims 18-22 are supported, for example, by original claims 11 and 14-17, respectively. Claim 19 is further supported by the specification, for example, the working Examples. Claim 23 is supported by original claims 13 and 16. Claim 24 is supported by original claims 13 and 17.

Claims 2-17 have been canceled.

Entry of the present Amendment is respectfully requested. Upon entry of the Amendment, claims 1 and 18-24 will be all the claims pending in the application.

In Paragraph No. 2 of the Office Action, claims 11-17 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

This rejection is moot because claims 11-17 have been canceled.

In Paragraph No. 3 of the Office Action, claims 1-17 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

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Applicants respectfully submit that the claim 1 as amended and newly added claims 18-24 fully comply with 35 U.S.C. § 112. In this Amendment, Applicants have canceled claims 2-17. In addition, as indicated above, amended claim 1 does not contain the term "general."

Regarding the term "medicament," Applicants respectfully submit that the term "medicament" means a medicine. See, for example, Stedman's Medical Dictionary.

In view of the above, the Examiner is respectfully requested to reconsider and withdraw the rejection.

In Paragraph No. 4 of the Office Action, claims 1-17 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sato et al (Journal of Medicinal Chemistry).

Applicants respectfully submit that the claim 1 as amended and newly added claims 18-24 are not obvious over Sato et al (Journal of Medicinal Chemistry) for the following reasons.

The present invention is directed to a compound which has a 5-HT<sub>3</sub> receptor activating action in addition to a 5-HT<sub>3</sub> receptor antagonistic activity. Attributable to these two kinds of pharmacological actions, the claimed compound effectively suppresses diarrhea, while causing no constipation as a side effect. Moreover, the claimed compound is metabolically stable.

Sato et al discloses that the compound 6s having a non-substituted piperazine ring has higher 5-HT<sub>3</sub> receptor "activating" action than the compound 6a having a piperazine ring substituted with a methyl group on the nitrogen atom of the piperazine ring. Sato et al. also discloses that the compound 6v having a methyl-substituted homopiperazine ring (which is the same compound as Compound E disclosed in EP '419) has more potent 5-HT<sub>3</sub> receptor "activating" action than the compounds 6a and 6s each having a piperazine ring, and that the

compound 6v shows higher suppressing action against diarrhea than granisetron as a control (Table 6).

However, Sato et al. neither teaches nor suggests that a higher 5-HT<sub>3</sub> receptor "antagonistic" activity can be obtained by modifying the substituent on the nitrogen atom of the homopiperazine ring. In other words, Sato et al. fails to teach any means to obtain a compound with higher 5-HT<sub>3</sub> receptor "antagonistic" activity. Accordingly, one of ordinary skill in the art would not have been motivated to substitute the methyl group of the compound 6v with a hydrogen atom to obtain a compound with higher 5-HT<sub>3</sub> receptor "antagonistic" activity in view of Sato et al. Further, one of ordinary skill in the art would not have reasonably expected that the removal of the methyl group on the homopiperazine ring of the compound 6v might increase 5-HT<sub>3</sub> receptor "antagonistic" activity.

In view of the above, the present invention is not obvious over Sato et al, and the rejection should be withdrawn.

In Paragraph No. 5 of the Office Action, claims 1-17 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over EP 806 419.

Applicants respectfully submit that claim 1 as amended and newly added claims 18-24 are not obvious over EP '419 for the following reasons.

EP '419 discloses benzoxazole compounds having a 5-HT<sub>3</sub> receptor activating action in addition to a 5-HT<sub>3</sub> receptor antagonistic activity. However, EP '419 fails to teach or suggest the metabolic stability of the compounds.

Further, as shown in Test Examples 2 and 4, the presently claimed compound not only

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has unexpectedly higher suppressing action against diarrhea than Compound E disclosed in EP '419 (which is the same compound as the compound 6v disclosed in Sato et al), but also is metabolically very stable. EP '419 does not disclose or suggest these advantageous features of the present invention.

In view of the above, the present invention is not obvious over EP '419, and the rejection should be withdrawn.

In Paragraph No. 6 of the Office Action, claim 14 is objected to as allegedly being in improper dependent form.

This objection is moot because claim 14 has been canceled.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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